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PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

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* * * * * * * * * *
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NEWS
NEWS
         NOV 21
                 CAS patent coverage to include exemplified prophetic
                 substances identified in English-, French-, German-,
                 and Japanese-language basic patents from 2004-present
NEWS
         NOV 26
                 MARPAT enhanced with FSORT command
NEWS
         NOV 26
                 CHEMSAFE now available on STN Easy
         NOV 26
NEWS
                 Two new SET commands increase convenience of STN
                 searching
NEWS
         DEC 01
                 ChemPort single article sales feature unavailable
      6
                 GBFULL now offers single source for full-text
NEWS
         DEC 12
                  coverage of complete UK patent families
NEWS
      8
         DEC 17
                 Fifty-one pharmaceutical ingredients added to PS
NEWS
         JAN 06
                 The retention policy for unread STNmail messages
                 will change in 2009 for STN-Columbus and STN-Tokyo
                 WPIDS, WPINDEX, and WPIX enhanced Japanese Patent
NEWS 10
         JAN 07
                 Classification Data
                 Simultaneous left and right truncation (SLART) added
NEWS 11 FEB 02
                 for CERAB, COMPUAB, ELCOM, and SOLIDSTATE
NEWS 12 FEB 02
                 GENBANK enhanced with SET PLURALS and SET SPELLING
NEWS 13 FEB 06
                 Patent sequence location (PSL) data added to USGENE
NEWS 14 FEB 10 COMPENDEX reloaded and enhanced
NEWS 15 FEB 11
                 WTEXTILES reloaded and enhanced
NEWS 16
         FEB 19
                 New patent-examiner citations in 300,000 CA/CAplus
                 patent records provide insights into related prior
                 art.
NEWS 17
         FEB 19
                 Increase the precision of your patent queries -- use
                 terms from the IPC Thesaurus, Version 2009.01
NEWS 18
         FEB 23
                 Several formats for image display and print options
                 discontinued in USPATFULL and USPAT2
         FEB 23
                 MEDLINE now offers more precise author group fields
NEWS 19
                 and 2009 MeSH terms
NEWS 20
         FEB 23
                 TOXCENTER updates mirror those of MEDLINE - more
                 precise author group fields and 2009 MeSH terms
NEWS 21
         FEB 23
                 Three million new patent records blast AEROSPACE into
                 STN patent clusters
NEWS 22
         FEB 25
                 USGENE enhanced with patent family and legal status
                 display data from INPADOCDB
NEWS 23
         MAR 06
                 INPADOCDB and INPAFAMDB enhanced with new display
                  formats
                 EPFULL backfile enhanced with additional full-text
NEWS 24
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NEWS EXPRESS JUNE 27 08 CURRENT WINDOWS VERSION IS V8.3,
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AND CURRENT DISCOVER FILE IS DATED 23 JUNE 2008.

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Enter NEWS followed by the item number or name to see news on that specific topic.

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FILE 'HOME' ENTERED AT 15:50:01 ON 16 MAR 2009

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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 15 MAR 2009 HIGHEST RN 1121544-94-2 DICTIONARY FILE UPDATES: 15 MAR 2009 HIGHEST RN 1121544-94-2

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TSCA INFORMATION NOW CURRENT THROUGH January 9, 2009.

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

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                             RO-4-6861 HYDROCHLORIDE/CN
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      ANSWER 1 OF 1 REGISTRY COPYRIGHT 2009 ACS on STN
T.1
       77848-04-5 REGISTRY
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CI
      MAN
LC
                      BIOSIS, CA, CAPLUS, TOXCENTER
      STN Files:
DT.CA CAplus document type: Journal RL.NP Roles from non-patents: BIOL (Biological study); USES (Uses)
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
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                     5 REFERENCES IN FILE CAPLUS (1907 TO DATE)
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      ANSWER 1 OF 1 REGISTRY COPYRIGHT 2009 ACS on STN
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RN
      29925-17-5 REGISTRY
      2-Imidazolidinone, 4-[(3-butoxy-4-methoxyphenyl)methyl]- (CA INDEX NAME)
OTHER CA INDEX NAMES:
      2-Imidazolidinone, 4-(3-butoxy-4-methoxybenzyl)- (8CI)
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OTHER NAMES:
CN
      4-(3-Butoxy-4-methoxy benzyl)-2-imidazolidinone
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CN 4-(3-Butoxy-4-methoxybenzyl)-2-imidazolidone
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CN DL-4-(3-Butoxy-4-methoxybenzyl)-2-imidazolidinone

CN R 020-1724

CN Ro 20-1724

CN Ro 20-174

CN Roche 20-1724

DR 34185-37-0, 391936-33-7

MF C15 H22 N2 O3

LC STN Files: AGRICOLA, BEILSTEIN\*, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CHEMCATS, CIN, CSCHEM, DDFU, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, PHAR, RTECS\*, TOXCENTER, USPAT2, USPATFULL (\*File contains numerically searchable property data)

DT.CA CAplus document type: Conference; Journal; Patent

RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PRP (Properties); RACT (Reactant or reagent); USES (Uses)

RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); USES (Uses)

RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)

RLD.NP Roles for non-specific derivatives from non-patents: BIOL (Biological study); PREP (Preparation)

\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

412 REFERENCES IN FILE CA (1907 TO DATE)

3 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

412 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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    ANSWER 1 OF 1 REGISTRY COPYRIGHT 2009 ACS on STN
RN
     61413-54-5 REGISTRY
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       MEDLINE, MRCK*, PHAR, PROMT, PROUSDDR, RTECS*, SYNTHLINE, TOXCENTER,
       USAN, USPAT2, USPATFULL
         (*File contains numerically searchable property data)
                     EINECS**, WHO
     Other Sources:
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(\*\*Enter CHEMLIST File for up-to-date regulatory information)

DT.CA Caplus document type: Conference; Dissertation; Journal; Patent

RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study);
PREP (Preparation); PROC (Process); PRP (Properties); PRPH (Prophetic);
RACT (Reactant or reagent); USES (Uses)

RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); USES (Uses)

RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)

RLD.NP Roles for non-specific derivatives from non-patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PRP (Properties); USES (Uses)

\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1188 REFERENCES IN FILE CA (1907 TO DATE)

22 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

1188 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> d his

(FILE 'HOME' ENTERED AT 15:50:01 ON 16 MAR 2009)

FILE 'REGISTRY' ENTERED AT 15:50:10 ON 16 MAR 2009

E "RO-1724"/CN 25 E "RO 1724"/CN 25

L1 1 S E3

E "RO 1724"/CN 25 E "RO 20-1724"/CN 25

L2 1 S E3

E "RO 20-1724"/CN 25

E "ROLIPRAM"/CN 25

L3 1 S E3

=> file medline caplus wpids uspatfull

COST IN U.S. DOLLARS

SINCE FILE TOTAL
ENTRY SESSION
24.12 24.34

FULL ESTIMATED COST

FILE 'MEDLINE' ENTERED AT 15:52:30 ON 16 MAR 2009

FILE 'CAPLUS' ENTERED AT 15:52:30 ON 16 MAR 2009
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FILE 'USPATFULL' ENTERED AT 15:52:30 ON 16 MAR 2009
CA INDEXING COPYRIGHT (C) 2009 AMERICAN CHEMICAL SOCIETY (ACS)

=> s 12 or 13

L4 3096 L2 OR L3

=> s 14 and (CLL or "chronic myelogenous leukemia")

L5 34 L4 AND (CLL OR "CHRONIC MYELOGENOUS LEUKEMIA")

=> s 15 and (prd<19980924 or pd<19980924)

'19980924' NOT A VALID FIELD CODE

1 FILES SEARCHED...

L6 2 L5 AND (PRD<19980924 OR PD<19980924)

=> d 16 1-2 ibib, abs

SOURCE:

L6 ANSWER 1 OF 2 MEDLINE on STN ACCESSION NUMBER: 1998421394 MEDLINE DOCUMENT NUMBER: PubMed ID: 9746789

TITLE: Type 4 cyclic adenosine monophosphate phosphodiesterase as

a therapeutic target in chronic lymphocytic leukemia.

AUTHOR: Kim D H; Lerner A

CORPORATE SOURCE: Department of Medicine, Section of Hematology and Oncology,

Boston Medical Center, Boston, MA 02118, USA.

Blood, (1998 Oct 1) Vol. 92, No. 7, pp. 2484-94.

Journal code: 7603509. ISSN: 0006-4971.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

(RESEARCH SUPPORT, NON-U.S. GOV'T)

LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals

ENTRY MONTH: 199810

ENTRY DATE: Entered STN: 29 Oct 1998

Last Updated on STN: 3 Mar 2000 Entered Medline: 19 Oct 1998

AB Theophylline, a drug known to inhibit several classes of adenosine 3'5' cyclic monophosphate (cAMP) phosphodiesterases (PDEs), induces apoptosis in chronic lymphocytic leukemia (CLL) cells. Because the PDE target for theophylline in CLL remains unknown, we examined the ability of isoform-specific PDE inhibitors to increase cAMP levels and induce apoptosis in primary CLL cells. Reverse transcriptase-polymerase chain reaction of purified CLL cDNA amplified transcripts for PDE1B, 4A and 4B. The type 4 PDE inhibitor rolipram but not the type 1 inhibitor vinpocetine increased CLL cAMP levels. Rolipram-inhibitable (type 4) but not calcium-calmodulin augmented (type 1) PDE enzyme activity was detected in CLL samples. In samples from 13 of 14 CLL patients, rolipram induced apoptosis in a dose-dependent fashion over a 48-hour period. Interleukin-2 (IL-2)-cultured whole mononuclear cells (WMC) and anti-Iq stimulated CD19(+) B cells were resistant to the induction of apoptosis by rolipram while unstimulated CD19(+) B cells, which had a high basal apoptotic rate, were more sensitive. Rolipram stimulated elevations in cAMP levels in all four of these cell populations, suggesting that they differed in sensitivity to cAMP-induced apoptosis. Consistent with this hypothesis, incubation with the cell permeable cAMP analog dibutyryl-cAMP induced apoptosis in CLL cells and unstimulated B cells but not in IL-2-cultured WMC or anti-Ig stimulated B cells. These data identify PDE4 as a family of enzymes whose inhibition induces apoptosis in CLL cells.

L6 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1998:646421 CAPLUS

DOCUMENT NUMBER: 130:261

TITLE: Type 4 cyclic adenosine monophosphate

phosphodiesterase as a therapeutic target in chronic

lymphocytic leukemia
AUTHOR(S):

Kim, Doo Ho; Lerner, Adam

CORPORATE SOURCE: Department of Medicine, Section of Hematology and

Oncology, Boston Medical Center, Boston, MA, 02118,

USA

SOURCE: Blood (1998), 92(7), 2484-2494 CODEN: BLOOAW; ISSN: 0006-4971

PUBLISHER: W. B. Saunders Co.

DOCUMENT TYPE: Journal LANGUAGE: English

Theophylline, a drug known to inhibit several classes of adenosine 3'5' cyclic monophosphate (cAMP) phosphodiesterases (PDEs), induces apoptosis in chronic lymphocytic leukemia (CLL) cells. Because the PDE target for theophylline in CLL remains unknown, the authors examined the ability of isoform-specific PDE inhibitors to increase cAMP levels and induce apoptosis in primary CLL cells. Reverse transcriptase-polymerase chain reaction of purified CLL cDNA amplified transcripts for PDE1B, 4A and 4B. The type 4 PDe inhibitor rolipram but not the type 1 inhibitor vinpocetine increased CLL cAMP levels. Rolipram-inhibitable (type 4) but not calcium-calmodulin augmented (type 1) PDE enzyme activity was detected in CLL samples. In samples from 13 of 14 CLL patients, rolipram induced apoptosis in a dose-dependent fashion over a 48-h period. Interleukin-2 (IL-2)-cultured whole mononuclear cells (WMC) and anti-Iq stimulated CD19+ B cells were resistant to the induction of apoptosis by rolipram while unstimulated CD19+ B cells, which had a high basal apoptotic rate, were more sensitive. Rolipram stimulated elevations in cAMP levels in all four of these cell populations, suggesting that they differed in sensitivity to cAMP-induced apoptosis. Consistent with this hypothesis, incubation with the cell permeable cAMP analog dibutyryl-cAMP induced apoptosis in CLL cells and unstimulated B cells but not in IL-2-cultured WMC or anti-Iq stimulated B cells. These data identify PDE4 as a family of enzymes whose inhibition induces apoptosis in CLL cells.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his

(FILE 'HOME' ENTERED AT 15:50:01 ON 16 MAR 2009)

FILE 'REGISTRY' ENTERED AT 15:50:10 ON 16 MAR 2009

E "RO-1724"/CN 25 E "RO 1724"/CN 25

L1 1 S E3

E "RO 1724"/CN 25 E "RO 20-1724"/CN 25

L2 1 S E3

E "RO 20-1724"/CN 25 E "ROLIPRAM"/CN 25

L3 1 S E3

FILE 'MEDLINE, CAPLUS, WPIDS, USPATFULL' ENTERED AT 15:52:30 ON 16 MAR 2009

L4 3096 S L2 OR L3

L5 34 S L4 AND (CLL OR "CHRONIC MYELOGENOUS LEUKEMIA")

L6 2 S L5 AND (PRD<19980924 OR PD<19980924)

=> s type(A)4(A)PDE(A)inhibitor

L7 35 TYPE(A) 4(A) PDE(A) INHIBITOR

=> s type(A)4(A)phosphodiesterase(A)inhibitor 201 TYPE(A) 4(A) PHOSPHODIESTERASE(A) INHIBITOR => s phosphodiesterase(A)type(A)4(A)inhibitor L9 145 PHOSPHODIESTERASE(A) TYPE(A) 4(A) INHIBITOR => s 17 and 18 and 19 11 L7 AND L8 AND L9 L10 => s 17 or 18 or 19 223 L7 OR L8 OR L9 => dup rem 111 PROCESSING COMPLETED FOR L11 152 DUP REM L11 (71 DUPLICATES REMOVED) => s 112 and (CLL or "chronic myelogenous leukemia") 7 L12 AND (CLL OR "CHRONIC MYELOGENOUS LEUKEMIA") T.13 => d 113 1-7 ibib, absL13 ANSWER 1 OF 7 MEDLINE on STN 2001540740 ACCESSION NUMBER: MEDLINE PubMed ID: 11587214 DOCUMENT NUMBER: Phosphodiesterase type 4 TITLE: inhibitor suppresses expression of anti-apoptotic members of the Bcl-2 family in B-CLL cells and induces caspase-dependent apoptosis. AUTHOR: Siegmund B; Welsch J; Loher F; Meinhardt G; Emmerich B; Endres S; Eigler A CORPORATE SOURCE: Division of Clinical Pharmacology, Medizinische Klinik Innenstadt, Klinikum of the Ludwig-Maximilians-University Munich, Germany. SOURCE: Leukemia: official journal of the Leukemia Society of America, Leukemia Research Fund, U.K, (2001 Oct) Vol. 15, No. 10, pp. 1564-71. Journal code: 8704895. ISSN: 0887-6924. PUB. COUNTRY: England: United Kingdom DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T) LANGUAGE: English FILE SEGMENT: Priority Journals ENTRY MONTH: 200202 ENTRY DATE: Entered STN: 8 Oct 2001 Last Updated on STN: 23 Feb 2002 Entered Medline: 22 Feb 2002 AB B cell chronic lymphocytic leukemia (B-CLL) is an incurable clonal disease which shows initial responsiveness to a number of chemotherapeutic drugs. However, in most patients the disease becomes resistant to treatment. Rolipram, a specific inhibitor of phosphodiesterase (PDE) type 4, the PDE predominantly expressed in B-CLL cells, has been shown to induce cAMP-dependent apoptosis in these cells. In the present study, we demonstrate that the extent of rolipram-induced apoptosis is similar to fludarabine-induced apoptosis in vitro. The combination of rolipram and fludarabine results in an enhancement in the number of apoptotic cells compared to apoptosis induced by either agent alone. Second, rolipram suppresses the expression of anti-apoptotic members of the Bcl-2 family and induces the pro-apoptotic protein Bax, thereby shifting the balance between pro- and anti-apoptotic members of the Bcl-2 family towards a pro-apoptotic direction. Finally

rolipram-induced apoptosis is caspase-dependent. PDE 4 inhibitors are currently under investigation for chronic obstructive pulmonary disease

and asthma in phase III clinical trials showing promising results with tolerable side-effects. In conclusion, by inducing apoptosis, by enhancing apoptosis induced by fludarabine, by suppressing Bcl-2, Bcl-X and by inducing Bax expression, PDE 4 inhibitors may add a new therapeutic option for patients with B-CLL.

L13 ANSWER 2 OF 7 MEDLINE on STN ACCESSION NUMBER: 1998421394 MEDLINE DOCUMENT NUMBER: PubMed ID: 9746789

TITLE: Type 4 cyclic adenosine monophosphate phosphodiesterase as

a therapeutic target in chronic lymphocytic leukemia.

AUTHOR: Kim D H; Lerner A

CORPORATE SOURCE: Department of Medicine, Section of Hematology and Oncology,

Boston Medical Center, Boston, MA 02118, USA.

SOURCE: Blood, (1998 Oct 1) Vol. 92, No. 7, pp. 2484-94.

Journal code: 7603509. ISSN: 0006-4971.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

(RESEARCH SUPPORT, NON-U.S. GOV'T)

LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals

ENTRY MONTH: 199810

ENTRY DATE: Entered STN: 29 Oct 1998

Last Updated on STN: 3 Mar 2000 Entered Medline: 19 Oct 1998

Theophylline, a drug known to inhibit several classes of adenosine 3'5' AB cyclic monophosphate (cAMP) phosphodiesterases (PDEs), induces apoptosis in chronic lymphocytic leukemia (CLL) cells. Because the PDE target for theophylline in CLL remains unknown, we examined the ability of isoform-specific PDE inhibitors to increase cAMP levels and induce apoptosis in primary CLL cells. Reverse transcriptase-polymerase chain reaction of purified CLL cDNA amplified transcripts for PDE1B, 4A and 4B. The type 4 PDE inhibitor rolipram but not the type 1 inhibitor vinpocetine increased CLL cAMP levels. Rolipram-inhibitable (type 4) but not calcium-calmodulin augmented (type 1) PDE enzyme activity was detected in CLL samples. In samples from 13 of 14 CLL patients, rolipram induced apoptosis in a dose-dependent fashion over a 48-hour period. Interleukin-2 (IL-2)-cultured whole mononuclear cells (WMC) and anti-Ig stimulated CD19(+) B cells were resistant to the induction of apoptosis by rolipram while unstimulated CD19(+) B cells, which had a high basal apoptotic rate, were more sensitive. Rolipram stimulated elevations in cAMP levels in all four of these cell populations, suggesting that they differed in sensitivity to cAMP-induced apoptosis. Consistent with this hypothesis, incubation with the cell permeable cAMP analog dibutyryl-cAMP induced apoptosis in CLL cells and unstimulated B cells but not in IL-2-cultured WMC or anti-Iq stimulated B cells. These data identify PDE4 as a family of enzymes whose inhibition induces apoptosis in CLL cells.

L13 ANSWER 3 OF 7 USPATFULL on STN

ACCESSION NUMBER: 2008:58534 USPATFULL

TITLE: Compositions and Methods for the Treatment of

Peripheral B-Cell Neoplasms

INVENTOR(S): Lerner, Adam, Newton, MA, UNITED STATES

Tiwari, Sanjay, Buchholz, GERMANY, FEDERAL REPUBLIC OF

PATENT ASSIGNEE(S): Trustees of Boston University, Boston, MA, UNITED

STATES, 02215 (U.S. corporation)

APPLICATION INFO.: US 2005-792172 A1 20051201 (11) WO 2005-US43613 20051201

20071106 PCT 371 date

NUMBER DATE \_\_\_\_\_

US 2004-632207P 20041201 (60) PRIORITY INFORMATION:

DOCUMENT TYPE: Utility FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: RONALD I. EISENSTEIN, 100 SUMMER STREET, NIXON PEABODY

LLP, BOSTON, MA, 02110, US

NUMBER OF CLAIMS: EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 9 Drawing Page(s) LINE COUNT: 1456

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

The present invention is directed to the use of a PDE4 inhibitor and a glucocorticoid to treat peripheral B-cell neoplasms. In particular, the present invention provides a method of treating individuals (e.g. patients) diagnosed with peripheral B-cell leukemias by administering pharmaceutical compositions comprising Type 4 cyclic adenosine monophosphate phosphodiesterase inhibitors and a glucocorticoid. Preferably, the combination of the PDE4 inhibitor and the glucocorticoid has a synergistic effect on apoptosis such that the level of apoptosis induced is greater than the level that would be expected by simply adding a PDE4 inhibitor to a glucocorticoid.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13 ANSWER 4 OF 7 USPATFULL on STN

ACCESSION NUMBER: 2006:315829 USPATFULL

TITLE: Method of modulating stress-activated protein kinase

system

Blatt, Lawrence M., San Francisco, CA, UNITED STATES INVENTOR(S):

Seiwert, Scott D., Pacifica, CA, UNITED STATES Beigelman, Leonid, San Mateo, CA, UNITED STATES

Radhakrishnan, Ramachandran, Fremont, CA, UNITED STATES

NUMBER KIND DATE PATENT INFORMATION: US 20060270612 A1 20061130 APPLICATION INFO.: US 2006-431132 A1 20060509 (11)

NUMBER DATE

US 2005-679471P 20050510 (60) US 2005-732230P 20051101 (60) PRIORITY INFORMATION:

DOCUMENT TYPE: Utility FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: KNOBBE MARTENS OLSON & BEAR LLP, 2040 MAIN STREET, FOURTEENTH FLOOR, IRVINE, CA, 92614, US

FOUNDER OF CLAIMS: 92
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS

NUMBER OF DRAWINGS: 7 Drawing Page(s)

LINE COUNT: 2814

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Disclosed are methods of modulating a stress activated protein kinase (SAPK) system with an active compound, wherein the active compound exhibits low potency for inhibition of at least one p38 MAPK; and wherein the contacting is conducted at a SAPK-modulating concentration that is at a low percentage inhibitory concentration for inhibition of the at least one p38 MAPK by the compound. Also disclosed are

derivatives of pirfenidone. These derivatives can modulate a stress activated protein kinase (SAPK) system.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13 ANSWER 5 OF 7 USPATFULL on STN

ACCESSION NUMBER: 2003:167754 USPATFULL

TITLE: Transgenic animal having a disrupted PDE7A gene and

uses thereof

INVENTOR(S): Michaeli, Tamar, Bronx, NY, UNITED STATES

KIND DATE NUMBER US 20030115615 A1 20030619 US 6740793 B2 20040525 PATENT INFORMATION: US 2001-950920 A1 20010912 (9) APPLICATION INFO.:

APPLICATION

DOCUMENT TYPE:

Utility

APPLICATION

LEGAL REPRESENTATIVE: Craig J. Arnold, Esq., AMSTER ROTHSTEIN & EBENSTEIN, 90
Park Avenue, New York, NY, 10016

NUMBER OF CLAIMS: 20 EXEMPLARY CLAIM:

NUMBER OF DRAWINGS: 4 Drawing Page(s)

1270 LINE COUNT:

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

The present invention provides a transgenic non-human animal whose genome comprises a disruption in its endogenous PDE7A gene, wherein the transgenic animal exhibits decreased expression of functional PDE7A protein relative to wild-type. The present invention further provides a method for creating a transgenic non-human animal exhibiting decreased expression of functional PDE7A protein relative to wild-type. Finally, the present invention provides a method for screening a PDE7A inhibitor for at least one side-effect.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13 ANSWER 6 OF 7 USPATFULL on STN

ACCESSION NUMBER: 2003:24171 USPATFULL

TITLE: Compositions and methods for the treatment of chronic

lymphocytic leukemia

INVENTOR(S): Lerner, Adam, Newton Highlands, MA, UNITED STATES PATENT ASSIGNEE(S): The Trustees of Boston University (U.S. corporation)

NUMBER KIND DATE US 20030018014 A1 20030123 US 2002-60759 A1 20020130 (10) PATENT INFORMATION: APPLICATION INFO.:

Division of Ser. No. US 2000-423349, filed on 1 May RELATED APPLN. INFO.:

2000, GRANTED, Pat. No. US 6399649 A 371 of

International Ser. No. WO 1999-US21518, filed on 17 Sep

1999, PENDING

NUMBER DATE -----

PRIORITY INFORMATION: US 1998-101721P 19980924 (60)

DOCUMENT TYPE:
FILE SEGMENT: Utility APPLICATION FILE SEGMENT:

LEGAL REPRESENTATIVE: NIXON PEABODY LLP, 101 FEDERAL ST, BOSTON, MA, 02110

NUMBER OF CLAIMS: 14 1 EXEMPLARY CLAIM:

NUMBER OF DRAWINGS: 14 Drawing Page(s)

LINE COUNT: 883 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Methods for treating patients with CLL with pharmaceutical agents are disclosed. The methods of the present invention can be used in patients that have not responded to standard treatment. In addition, the methods can be used to augment the impact of standard chemotherapy.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13 ANSWER 7 OF 7 USPATFULL on STN

ACCESSION NUMBER: 2002:129999 USPATFULL

TITLE: Compositions and methods for the treatment of chronic

lymphocytic leukemia

INVENTOR(S): Lerner, Adam, Newton Highlands, MA, United States

PATENT ASSIGNEE(S): Boston Medical Center Corporation, Boston, MA, United

States (U.S. corporation)

NUMBER DATE

PRIORITY INFORMATION: US 1998-101721P 19980924 (60)

DOCUMENT TYPE: Utility FILE SEGMENT: GRANTED

PRIMARY EXAMINER: Goldberg, Jerome D. LEGAL REPRESENTATIVE: Nixon Peabody LLP

NUMBER OF CLAIMS: 7
EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 26 Drawing Figure(s); 14 Drawing Page(s)

LINE COUNT: 901

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Methods for treating patients with CLL with pharmaceutical agents are disclosed. The methods of the present invention can be used in patients that have not responded to standard treatment. In addition, the methods can be used to augment the impact of standard chemotherapy.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d his

(FILE 'HOME' ENTERED AT 15:50:01 ON 16 MAR 2009)

FILE 'REGISTRY' ENTERED AT 15:50:10 ON 16 MAR 2009

E "RO-1724"/CN 25 E "RO 1724"/CN 25

L1 1 S E3

E "RO 1724"/CN 25 E "RO 20-1724"/CN 25

L2 1 S E3

E "RO 20-1724"/CN 25 E "ROLIPRAM"/CN 25

L3 1 S E3

FILE 'MEDLINE, CAPLUS, WPIDS, USPATFULL' ENTERED AT 15:52:30 ON 16 MAR 2009

L4 3096 S L2 OR L3

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34 S L4 AND (CLL OR "CHRONIC MYELOGENOUS LEUKEMIA")
             2 S L5 AND (PRD<19980924 OR PD<19980924)
1.6
T.7
             35 S TYPE(A)4(A)PDE(A)INHIBITOR
Г8
            201 S TYPE (A) 4 (A) PHOSPHODIESTERASE (A) INHIBITOR
1.9
           145 S PHOSPHODIESTERASE (A) TYPE (A) 4 (A) INHIBITOR
L10
            11 S L7 AND L8 AND L9
L11
            223 S L7 OR L8 OR L9
            152 DUP REM L11 (71 DUPLICATES REMOVED)
L12
L13
              7 S L12 AND (CLL OR "CHRONIC MYELOGENOUS LEUKEMIA")
=> s type(N)4(N)cyclic(N)adenosine(N)monophosphate(N)phosphodiesterase
            22 TYPE(N) 4(N) CYCLIC(N) ADENOSINE(N) MONOPHOSPHATE(N) PHOSPHODIES
               TERASE
\Rightarrow s 114 and (prd<19980924 or pd<19980924)
'19980924' NOT A VALID FIELD CODE
   1 FILES SEARCHED...
             3 L14 AND (PRD<19980924 OR PD<19980924)
=> d 115 1-3 ibib, abs
L15 ANSWER 1 OF 3
                       MEDLINE on STN
ACCESSION NUMBER:
                    1998421394
                                   MEDLINE
                    PubMed ID: 9746789
DOCUMENT NUMBER:
TITLE:
                    Type 4 cyclic
                    adenosine monophosphate
                    phosphodiesterase as a therapeutic target in
                    chronic lymphocytic leukemia.
AUTHOR:
                    Kim D H; Lerner A
CORPORATE SOURCE:
                    Department of Medicine, Section of Hematology and Oncology,
                    Boston Medical Center, Boston, MA 02118, USA.
                    Blood, (1998 Oct 1) Vol. 92, No. 7, pp. 2484-94.
SOURCE:
                    Journal code: 7603509. ISSN: 0006-4971.
PUB. COUNTRY:
                    United States
DOCUMENT TYPE:
                    Journal; Article; (JOURNAL ARTICLE)
                    (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE:
                    English
FILE SEGMENT:
                    Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH:
                    199810
ENTRY DATE:
                    Entered STN: 29 Oct 1998
                    Last Updated on STN: 3 Mar 2000
                    Entered Medline: 19 Oct 1998
AB
     Theophylline, a drug known to inhibit several classes of adenosine 3'5'
     cyclic monophosphate (cAMP) phosphodiesterases (PDEs), induces apoptosis
     in chronic lymphocytic leukemia (CLL) cells. Because the PDE target for
     theophylline in CLL remains unknown, we examined the ability of
     isoform-specific PDE inhibitors to increase cAMP levels and induce
     apoptosis in primary CLL cells. Reverse transcriptase-polymerase chain
     reaction of purified CLL cDNA amplified transcripts for PDE1B, 4A and 4B.
     The type 4 PDE inhibitor rolipram but not the type 1 inhibitor vinpocetine
     increased CLL cAMP levels. Rolipram-inhibitable (type 4) but not
     calcium-calmodulin augmented (type 1) PDE enzyme activity was detected in
     CLL samples. In samples from 13 of 14 CLL patients, rolipram induced
     apoptosis in a dose-dependent fashion over a 48-hour period.
     Interleukin-2 (IL-2)-cultured whole mononuclear cells (WMC) and anti-Ig
     stimulated CD19(+) B cells were resistant to the induction of apoptosis by
     rolipram while unstimulated CD19(+) B cells, which had a high basal
     apoptotic rate, were more sensitive. Rolipram stimulated elevations in
     cAMP levels in all four of these cell populations, suggesting that they
     differed in sensitivity to cAMP-induced apoptosis. Consistent with this
     hypothesis, incubation with the cell permeable cAMP analog dibutyryl-cAMP
     induced apoptosis in CLL cells and unstimulated B cells but not in
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T.5

IL-2-cultured WMC or anti-Ig stimulated B cells. These data identify PDE4 as a family of enzymes whose inhibition induces apoptosis in CLL cells.

L15 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1998:646421 CAPLUS

DOCUMENT NUMBER: 130:261

TITLE: Type 4 cyclic

adenosine monophosphate

phosphodiesterase as a therapeutic target in

chronic lymphocytic leukemia Kim, Doo Ho; Lerner, Adam

AUTHOR(S): Kim, Doo Ho; Lerner, Adam

CORPORATE SOURCE: Department of Medicine, Section of Hematology and

Oncology, Boston Medical Center, Boston, MA, 02118,

USA

SOURCE: Blood (1998), 92(7), 2484-2494

CODEN: BLOOAW; ISSN: 0006-4971

PUBLISHER: W. B. Saunders Co.

DOCUMENT TYPE: Journal LANGUAGE: English

Theophylline, a drug known to inhibit several classes of adenosine 3'5' cyclic monophosphate (cAMP) phosphodiesterases (PDEs), induces apoptosis in chronic lymphocytic leukemia (CLL) cells. Because the PDE target for theophylline in CLL remains unknown, the authors examined the ability of isoform-specific PDE inhibitors to increase cAMP levels and induce apoptosis in primary CLL cells. Reverse transcriptase-polymerase chain reaction of purified CLL cDNA amplified transcripts for PDE1B, 4A and 4B. The type 4 PDe inhibitor rolipram but not the type 1 inhibitor vinpocetine increased CLL cAMP levels. Rolipram-inhibitable (type 4) but not calcium-calmodulin augmented (type 1) PDE enzyme activity was detected in CLL samples. In samples from 13 of 14 CLL patients, rolipram induced apoptosis in a dose-dependent fashion over a 48-h period. Interleukin-2 (IL-2)-cultured whole mononuclear cells (WMC) and anti-Iq stimulated CD19+ B cells were resistant to the induction of apoptosis by rolipram while unstimulated CD19+ B cells, which had a high basal apoptotic rate, were more sensitive. Rolipram stimulated elevations in cAMP levels in all four of these cell populations, suggesting that they differed in sensitivity to cAMP-induced apoptosis. Consistent with this hypothesis, incubation with the cell permeable cAMP analog dibutyryl-cAMP induced apoptosis in CLL cells and unstimulated B cells but not in IL-2-cultured WMC or anti-Iq stimulated B cells. These data identify PDE4 as a family of enzymes whose inhibition induces apoptosis in CLL cells.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 3 OF 3 USPATFULL on STN

ACCESSION NUMBER: 2002:206794 USPATFULL

TITLE: Nicotinamide acids, amides, and their mimetics active

as inhibitors of PDE4 isozymes

INVENTOR(S): Magee, Thomas Victor, Mystic, CT, UNITED STATES

Marfat, Anthony, Mystic, CT, UNITED STATES

Chambers, Robert James, Mystic, CT, UNITED STATES

<--

PATENT ASSIGNEE(S): Pfizer Inc. (U.S. corporation)

PRIORITY INFORMATION: US 2001-265240P 20010131 (60) US 1997-43403P 19970404 (60)

US 1998-105120P 19981021 (60) Utility DOCUMENT TYPE: FILE SEGMENT: APPLICATION PFIZER INC, 150 EAST 42ND STREET, 5TH FLOOR - STOP 49, LEGAL REPRESENTATIVE: NEW YORK, NY, 10017-5612 NUMBER OF CLAIMS: 22 EXEMPLARY CLAIM: 1 7710 LINE COUNT: CAS INDEXING IS AVAILABLE FOR THIS PATENT. Compounds useful as inhibitors of PDE4 in the treatment of diseases regulated by the activation and degranulation of eosinophils, especially asthma, chronic bronchitis, and chronic obstructuive pulmonary disease, of the formula: ##STR1## wherein j is 0 or 1, k is 0 or 1, m is 0, 1, or 2; n is 1 or 2; A is selected from the partial Formulas: ##STR2## where q is 1, 2, or 3, W.sup.3 is --O--; --N(R.sup.9)--; or --OC(.dbd.O) --; R.sup.7 is selected from --H; --(C.sub.1-C.sub.6) alkyl, --(C.sub.2-C.sub.6) alkenyl, or --(C.sub.2-C.sub.6) alkynyl substituted by 0 to 3 substituents R.sup.10; --(CH.sub.2).sub.u--(C.sub.3-C.sub.7) cycloalkyl where u is 0, 1 or 2, substituted by 0 to 3 R.sup.10; and phenyl or benzyl substituted by 0 to 3 R.sup.14; R.sup.8 is tetrazol-5-yl; 1,2,4-triazol-3-yl; 1,2,4-triazol-3-on-5-yl; 1,2,3-triazol-5-yl; imidazol-2-yl; imidazol-4-yl; imidazolidin-2-on-4-yl; 1,3,4-oxadiazolyl; 1,3,4-oxadiazol-2-on-5-yl; 1,2,4-oxadiazol-3-yl; 1,2,4-oxadiazol-5-on-3-yl; 1,2,4-oxadiazol-5-yl; 1,2,4-oxadiazol-3-on-5-yl; 1,2,5-thiadiazolyl; 1,3,4-thiadiazolyl; morpholinyl; parathiazinyl; oxazolyl; isoxazolyl; thiazolyl; isothiazolyl; pyrrolyl; pyrazolyl; succinimidyl; glutarimidyl; pyrrolidonyl; 2-piperidonyl; 2-pyridonyl; 4-pyridonyl; pyridazin-3-onyl; pyridyl; pyrimidinyl; pyrazinyl; pyridazinyl; indolyl; indolinyl; isoindolinyl; benzo[b]furanyl; 2,3-dihydrobenzofuranyl; 1,3-dihydroisobenzofuranyl; 2H-1-benzopyranyl; 2-H-chromenyl; chromanyl; benzothienyl; 1H-indazolyl; benzimidazolyl; benzoxazolyl; benzisoxazolyl; benzothiazolyl; benzotriazolyl; benzotriazinyl; phthalazinyl; 1,8-naphthyridinyl; quinolinyl; isoquinolinyl; quinazolinyl; quinoxalinyl; pyrazolo[3,4-d]pyrimidinyl; pyrimido[4,5-d]pyrimidinyl; imidazo[1,2-a]pyridinyl; pyridopyridinyl; pteridinyl; or 1H-purinyl; or A is selected from phosphorous and sulfur acid groups; W is --0--; --S(.dbd.0).sub.t--, where t is 0, 1, or 2; or --N(R.sup.3)--; Y is .dbd.C(R.sup.1.sub.a)--, or --[N(O).sub.k] where k is 0 or 1; R.sup.4, R.sup.5 and R.sup.6 are (1) --H; provided that R.sup.5 and R.sup.6 are not both --H at the same time, --F; --Cl; -- (C.sub.2-C.sub.4) alkynyl; -- R.sup.16; -- OR.sup.16; --S(.dbd.0).sub.pR.sup.16; --C(.dbd.0)R.sup.16, --C(.dbd.0)OR.sup.16, --C(.dbd.0)OR.sup.16; --OC(.dbd.0)R.sup.16; --CN; --NO.sub.2; --C(.dbd.0)NR.sup.16R.sup.17; --OC(.dbd.0)NR.sup.16R.sup.17; --NR.sup.12.sub.aC(.dbd.0)NR.sup.16R.sup.17; --NR.sup.12.sub.aC(.dbd.NR.sup.12)NR.sup.16R.sup.17; --NR.sup.12.sub.aC(.dbd.NCN)NR.sup.16R.sup.16; --NR.sup.12.sub.aC(.dbd.N--NO.sub.2)NR.sup.15R.sup.16; --C(.dbd.NR.sup.12.sub.a) NR.sup.15R.sup.16; --CH.sub.2C(.dbd.NR.sup.12.sub.a)NR.sup.16R.sup.17; --OC(.dbd.NR.sup.12.sub.a)NR.sup.16R.sup.17; --OC(.dbd.N--NO.sub.2)NR.sup.16R.sup.17; --NR.sup.16R.sup.17; --CH.sub.2NR.sup.16R.sup.17; --NR.sup.12.sub.aC(.dbd.0)R.sup.16; --NR.sup.12.sub.aC(.dbd.0)OR.sup.16; .dbd.NOR.sup.16; --NR.sup.12.sub.aS(.dbd.0).sub.pR.sup.17

--S(.dbd.O).sub.pNR.sup.16R.sup.17; and

--CH.sub.2C(.dbd.NR.sup.12.sub.a)NR.sup.16R.sup.17; (2)

--(C.sub.1-C.sub.4) alkyl including dimethyl and --(C.sub.1-C.sub.4)

alkoxy substituted with 0 to 3 substituents --F or --Cl; or 0 or 1 substituent (C.sub.1-C.sub.2) alkoxycarbonyl-, (C.sub.1-C.sub.2) alkylcarbonyl-, or (C.sub.1-C.sub.2) alkylcarbonyloxy-; or (3) an aryl or heterocyclic moiety; or (4) R.sup.5 and R.sup.6 are taken together to form a moiety of partial Formulas (1.3.1) through (1.3.15): ##STR3##

or a pharmaceutically acceptable salt thereof.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> s inhibitor(N)PDE4

L16 1973 INHIBITOR(N) PDE4

=> s 116 and (CLL or "chronic myelogenous leukemia")

17 78 L16 AND (CLL OR "CHRONIC MYELOGENOUS LEUKEMIA")

 $\Rightarrow$  s 117 and (prd<19980924 or pd<19980924)

'19980924' NOT A VALID FIELD CODE

1 FILES SEARCHED...

L18 2 L17 AND (PRD<19980924 OR PD<19980924)

=> d 118 1-2 ibib, abs

L18 ANSWER 1 OF 2 USPATFULL on STN

ACCESSION NUMBER: 2003:265926 USPATFULL

TITLE: Substituted gamma-phenyl-delta-lactams and uses related

thereto

INVENTOR(S): Shen, Yaping, Port Coquitlam, CANADA

NUMBER

Burgoyne, David L., Delta, CANADA

Lauener, Ronald W., New Westminster, CANADA

Zhou, Yuanlin, Richmond, CANADA

Rebstein, Patrick J., Vancouver, CANADA Abraham, Samuel D. M., Vancouver, CANADA

KIND

DATE

PATENT ASSIGNEE(S): Inflazyme Pharmaceuticals Ltd., Richmond, BC, CANADA,

V6V 2M2 (non-U.S. corporation)

PATENT INFORMATION:	US 20030186943 A1 20031002				
	US 6770658 B2 20040803				
APPLICATION INFO.:	US 2002-263336 A1 20021001 (10)				
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 2001-786949, filed				
	on 11 May 2001, GRANTED, Pat. No. US 6458829 A 371 of				
	International Ser. No. WO 1999-CA819, filed on 9 Sep 1999, UNKNOWN Continuation-in-part of Ser. No. US				
	2002-81993, filed on 22 Feb 2002, PENDING Continuation				
	of Ser. No. US 2000-527699, filed on 16 Mar 2000,				
	ABANDONED Continuation of Ser. No. US 1999-393445,				
	filed on 8 Sep 1999, ABANDONED				

	NUMBER	DATE	
PRIORITY INFORMATION:	US 1998-99637P US 1999-121507P US 1999-149517P	19980909 19990223 19990817	(60)
DOCUMENT TYPE: FILE SEGMENT:	Utility APPLICATION		(00)

LEGAL REPRESENTATIVE: SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH

AVE, SUITE 6300, SEATTLE, WA, 98104-7092

NUMBER OF CLAIMS: 49 EXEMPLARY CLAIM: 1 LINE COUNT: 6094

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

 $\gamma$ -Phenyl-substituted  $\Delta$ -lactams are disclosed. They may be

formulated into pharmaceutical compositions, and/or used in the

treatment or prevention of inflammation or other conditions or disease

states.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L18 ANSWER 2 OF 2 USPATFULL on STN

ACCESSION NUMBER: 2002:254380 USPATFULL

TITLE: Substituted  $\gamma$ -phenyl- $\Delta$ -lactones and analogs

thereof and uses related thereto

INVENTOR(S): Shen, Yaping, Port Coquitlam, CANADA Burgoyne, David L., Delta, CANADA

Lauener, Ronald W., Westminister, CANADA

Zhou, Yuanlin, Richmond, CANADA

Rebstein, Patrick J., Vancouver, CANADA Abraham, Samuel D. M., Vancouver, CANADA

PATENT ASSIGNEE(S): Inflazyme Pharmaceuticals Ltd., Richmond, CANADA

(non-U.S. corporation)

	NUMBER	KIND	DATE		
PATENT INFORMATION:	US 6458829	B1	20021001		
	WO 2000014083		20000316		
APPLICATION INFO.:	US 2001-786949		20010511	(9)	
	WO 1999-CA819		19990909		
			20010511	PCT 371	date

NUMBER	DATE

US 1999-149517P 19990817 (60) US 1999-121507P 19990223 (60) PRIORITY INFORMATION:

US 1998-99637P 19980909 (60) <--

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PRIMARY EXAMINER: Owens, Amelia

LEGAL REPRESENTATIVE: Seed Intellectual Property Law Group PLLC

NUMBER OF CLAIMS: 63 EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 0 Drawing Figure(s); 0 Drawing Page(s)

LINE COUNT: 5553

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

 $\gamma$ -Phenyl-substituted  $\Delta$ -lactones and analogs thereof, AB

including lactams, are disclosed. They may be formulated into

pharmaceutical compositions, and/or used in the treatment or prevention

of inflammation or other conditions or disease states.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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FILE 'REGISTRY' ENTERED AT 15:50:10 ON 16 MAR 2009

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E "RO 1724"/CN 25

L1 1 S E3

E "RO 1724"/CN 25

E "RO 20-1724"/CN 25

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              1 S E3
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L9
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